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EXAMINER

CHAKRABARTI, ARUN K

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 10/08/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/616,787

Applicant(s)

ENGLERT, DAVID F.

Examiner

Arun Chakrabarti

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 August 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 36-43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6 and 36-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *Detailed Action*.

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DETAILED ACTION

Continued Examination Under 37 CAR 1.114

1. A request for continued examination under 37 CAR 1.114, including the fee set forth in 37 CAR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CAR 1.114, and the fee set forth in 37 CAR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CAR 1.114. Applicant's submission filed on July 29, 2002 has been entered.

Specification

2. Claim 1 has been amended and new claims 42-43 have been added.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

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4. Claims 1-3, 5 and 36 are rejected under 35 U.S.C. 102 (e) as being anticipated by Coull et al. (U.S. Patent 6,361,942 B1) (March 26, 2002).

Coull et al. teaches a method for multiplexed analysis of a plurality of target nucleic acid sequences in a sample (Column 18, line 20 to Column 20, line 14) comprising the methods of:

providing, for each target nucleic acid sequence to be analyzed, at least one probe/primer molecule which probe/primer molecule includes a region of sequence substantially complementary to a sequence in the target nucleic acid sequence and a region that is not located at either terminus of the probe/primer and which includes a capture tag sequence (Figures 20 and 21);

forming a reaction mixture which includes the probe/primer molecules and the target sequences under conditions such that, if a probe/primer molecule specific for a target sequence and the target sequences are both present, one or a plurality of derivative molecules having a capture tag at one or both its 3' or 5' termini, of the probe specific for the target sequence, is generated, and evaluating the presence of one or more derivative molecules, each derivative molecule indicating a target nucleic acid sequence in the sample, thereby analyzing the plurality of target nucleic acid sequences in the sample (Column 18, line 20 to Column 20, line 14);

evaluating the presence of one or more capture sequence tags (Column 18, line 20 to Column 20, line 14 and Examples 14-18).

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Coull et al. teaches a method wherein the derivative nucleic acid molecules are analyzed by hybridizing the tag sequences to capture probes which are spatially separated (Examples 14-18).

Coull et al. inherently teaches a method wherein the capture probes are partially duplex probes with capture-tag-complementary single stranded overhangs (Examples 14-18).

Coull et al. teaches a method wherein the capture tags are disposed on beads ().

Coull et al. teaches a method wherein the capture tags are disposed on an ordered array (Figures 1B and 1C and Column 20, line 66 to column 21, line 65).

Coull et al. teaches a method wherein the probe/primer molecule comprises a restriction endonuclease recognition site (Example 18, Column 72, lines 63-67).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claim 4 is rejected under 35 U.S.C. 103 (a) over Coull et al. (U.S. Patent 6,361,942 B1) (March 26, 2002) in view of Wong (U.S. Patent 5,935,793) (August 10, 1999)..

Coull et al. teaches the methods of claims 1-3, 5 and 36 as described above.

Coull et al. does not teach the method wherein the capture tags are disposed on beads.

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Wong teaches a method wherein the capture tags are disposed on beads (Column 22, lines 7-12).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a method wherein the capture tags are disposed on beads of Wong into the method of Coull et al., since Wong states, "Preferably, each fraction is collected onto an adsorbent layer or membrane (e.g., a layer of magnetic beads on a porous membrane near the top of each collection well or vial) that binds the sequencing fragments while allowing non-oligonucleotide materials (e.g., electrolytes and small molecules) to pass through (Column 22, lines 7-12)." By employing scientific reasoning, an ordinary artisan would have combined and substituted a method wherein the capture tags are disposed on beads of Wong into the method of Coull et al. in order to improve the analysis of a plurality of target nucleic acid. An ordinary practitioner would have been motivated to combine and substitute a method wherein the capture tags are disposed on beads of Wong into the method of Coull et al., in order to achieve the express advantages noted by Wong, of a method that provides an adsorbent layer or membrane (e.g., a layer of magnetic beads on a porous membrane near the top of each collection well or vial) that binds the sequencing fragments while allowing non-oligonucleotide materials (e.g., electrolytes and small molecules) to pass through.

7. Claim 6 is rejected under 35 U.S.C. 103 (a) over Coull et al. (U.S. Patent 6,361,942 B1) (March 26, 2002) in view of Zhang et al. (U.S. Patent 5,942,391) (August 24, 1991).

Coull et al. teaches the methods of claims 1-3, 5 and 36 as described above.

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Coull et al. does not teach the method wherein the derivative nucleic acid is ligated to a capture probe and then washed.

Zhang et al. teach the method wherein the derivative nucleic acid is washed and then ligated to a capture probe. (Column 40, lines 1-27 and Figure 5). However, MPEP 2144.04 further states, “*In re Gibson*, 39 F.2d 975, 5 USPQ 230 (CCPA 1930) Selection of any order of mixing ingredients is *prima facie* obvious”.

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the washing and ligation steps of Zhang et al. into the method of Coull et al., since Zhang et al. state, “The beads were then washed twice with washing buffer to remove nonhybridized probes, as well as GnSCN, proteins, nucleic acids, and any potential PCR inhibitors (Column 40, lines 4-8).” By employing scientific reasoning, an ordinary artisan would have combined and substituted the washing and ligation steps of Zhang et al. into the method of Coull et al. in order to improve the analysis of a plurality of target nucleic acid. An ordinary practitioner would have been motivated to combine and substitute the washing and ligation steps of Zhang et al. into the method of Coull et al., in order to achieve the express advantages noted by Zhang et al., of a method that provides removal of nonhybridized probes, as well as GnSCN, proteins, nucleic acids, and any potential PCR inhibitors.

8. Claims 37-40, and 42-43 are rejected under 35 U.S.C. 103 (a) over Coull et al. (U.S. Patent 6,361,942 B1) (March 26, 2002) in view of Sorge et al. (U.S. Patent 6,261,797 B1) (July 17, 2001).

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Coull et al. teaches the methods of claims 1-3, 5 and 36 as described above.

Coull et al. does not teach the method wherein the cleavage of the probe/primer molecule with the restriction endonuclease leaves the capture tag sequence in a single-stranded overhang.

Sorge et al teach the method wherein the cleavage of the probe/primer molecule with the restriction endonuclease leaves the capture tag sequence in a single-stranded overhang (Column 7, lines 6-25)

Coull et al. does not teach the method wherein the endonuclease recognition site is a Type IIS restriction endonuclease recognition site.

Sorge et al teach the method wherein the endonuclease recognition site is a Type IIS restriction endonuclease recognition site.(Column 5, line 5 to column 6, line 48).

Coull et al. does not teach the method wherein the forming comprises cleaving probe/primer molecules that are annealed to target sequences with a Type IIS restriction endonuclease.

Sorge et al teach the method wherein the forming comprises cleaving probe/primer molecules that are annealed to target sequences with a Type IIS restriction endonuclease.(Column 5, line 5 to column 6, line 48)

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method wherein the endonuclease recognition site is a Type IIS restriction endonuclease recognition site of Sorge et al. into the method of Coull et al., since Sorge et al. state, "Particularly preferred are sites recognized by

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Type IIS restriction endonucleases. When these primers are used to amplify a polynucleotide product, and then treated with Type IIS restriction endonucleases, the polynucleotide sequence in the synthesized product which comprise the type IIS recognition sequence are completely or partially removed. Thus, using the methods of the invention, one may efficiently synthesize and manipulate polynucleotides of interest by primer mediated polynucleotide synthesis, e.g., PCR, without introducing some or all of the primer-derived nucleotides into the ultimate synthesis products (Column 5, lines 15-26).” By employing scientific reasoning, an ordinary artisan would have combined and substituted the method wherein the endonuclease recognition site is a Type IIS restriction endonuclease recognition site of Sorge et al. into the method of Coull et al., in order to improve the analysis of a plurality of target nucleic acid. An ordinary practitioner would have been motivated to combine and substitute the method wherein the endonuclease recognition site is a Type IIS restriction endonuclease recognition site of Sorge et al. into the method of Coull et al., in order to achieve the express advantages noted by Sorge et al., of an invention that provides particularly preferred sites recognized by Type IIS restriction endonucleases and the methods by which one may efficiently synthesize and manipulate polynucleotides of interest by primer mediated polynucleotide synthesis, e.g., PCR, without introducing some or all of the primer-derived nucleotides into the ultimate synthesis products.

9. Claim 41 is rejected under 35 U.S.C. 103 (a) over Coull et al. (U.S. Patent 6,361,942 B1) (March 26, 2002) in view of Matsui et al. (U.S. Patent 6,255,081 B1) (July 3, 2001).

Coull et al. teaches the methods of claims 1-3, 5 and 36 as described above.

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Coull et al. does not teach the method wherein the forming comprises cleaving probe/primer molecules with a flap endonuclease.

Matsui et al. teach the method wherein the forming comprises cleaving probe/primer molecules with a flap endonuclease (Abstract, Claims 1-8, and Examples 6-9).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method wherein the forming comprises cleaving probe/primer molecules with a flap endonuclease of Matsui et al. into the method of Coull et al., since Matsui et al. state, "Further, this enzyme is thermally stable, so it becomes possible to develop new techniques of conducting artificial homologous recombination of genetic shuffling highly efficiently by coupling the enzyme reaction with PCR (Abstract, last sentence)." By employing scientific reasoning, an ordinary artisan would have combined and substituted the method wherein the forming comprises cleaving probe/primer molecules with a flap endonuclease of Matsui et al. into the method of Coull et al. in order to improve the analysis of a plurality of target nucleic acid. An ordinary practitioner would have been motivated to combine and substitute the method wherein the forming comprises cleaving probe/primer molecules with a flap endonuclease of Matsui et al. into the method of Coull et al., in order to achieve the express advantages noted by Matsui et al., of a thermally stable enzyme, so that it becomes possible to develop new techniques of conducting artificial homologous recombination of genetic shuffling highly efficiently by coupling the enzyme reaction with PCR.

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Response to Amendment

10. In response to amendment, previous 102(e) rejection has been withdrawn. However, a new 102 (e) rejection and new 103 (a) rejections based on the new 102(e) rejection have been included.

Response to Arguments

11. Applicant's arguments with respect to all pending claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

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Arun Chakrabarti,

Patent Examiner,

September 4, 2002



W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600